Docket No. 7444/73871/GJG/BJA

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants : Andrzej Lipkowski et al.

Serial No. : 10/524,343 (a §371 of PCT International Application NO. PCT/PL2003/000077) Examiner: Julie Ha

Filed : January 30, 2006 Group Art Unit: 1654

For : COMPOUNDS AND THEIR ANALGESIC APPLICATIONS

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Commissioner for Patents
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SIR:

DECLARATION UNDER 37 C.F.R. §1.132 OF ANDRZEJ W. LIPKOWSKI

I, Andrzej W. Lipkowski, hereby declare that:

1. I am named as an inventor on the above-identified application and I am employed as a Professor at the Medical Research Center, Polish Academy of Sciences, Pawinskiego 5, PL 02-106 Warsawza, Poland.

2. Experiments were performed by me or under my supervision using a rat tail-flick model of anti-nociception to determine the duration of anti-nociception of each of (1) Tyr-D-Met-Gly-Phe-NH_2; (2) (Tyr-D-Met-Gly-Phe-NH-)$_2$; (3) Tyr-D-Ala-Gly-Phe-NH_2; and (4) (Tyr-D-Ala-Gly-Phe-NH-)$_2$.

3. We found the duration of anti-nociception of the two

monomers, namely Tyr-D-Met-Gly-Phe-NH_2 and Tyr-D-Ala-Gly-Phe-NH_2, to be comparable for the same dosage tested.

4. We found the level of anti-nociception elicited by 0.005 nmol biphalin, i.e. the dimer (Tyr-D-Ala-Gly-Phe-NH-)$_2$, to be 30% Maximum Possible Effect (MPE) at 30 minutes after administration and equivalent to 0% MPE at 120 minutes after administration.

5. We found the level of anti-nociception elicited by 0.005 nmol of the dimer (Tyr-D-Met-Gly-Phe-NH-)$_2$ to be 55% MPE at 30 minutes after administration of the dimer and 30% MPE at 120 minutes after administration. Attached hereto as **Exhibit A** is a graphical representation of the results comparing the Tyr-D-Met-Gly-Phe-NH_2 monomer, (1.0 nmol), and the dimer (Tyr-D-Met-Gly-Phe-NH-)$_2$, (0.005 nmol), in the rat tail-flick model of anti-nociception.

6. Accordingly, although the duration of anti-nociception of the monomers was comparable, the dimer (Tyr-D-Met-Gly-Phe-NH-)$_2$ was still eliciting substantial anti-nociception at 120 minutes after administration, which is improved over and is not comparable to the duration of anti-nociception achieved with the biphalin dimer.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made herein on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false

statements and the like so made are punishable by fine or imprisonment, or both, under section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the subject application or any patent issuing thereon.

Dated: March 28, 2007

Andrzej W. Lipkowski

Tyr-D-Met-Gly-Phe-NH_2 vs. [Tyr-D-Met-Gly-Phe-NH-]$_2$

rats, intrathecal